

**REMARKS**

Claims 51-105 were withdrawn from consideration in Applicants' amendment dated July 23, 2001. These claims have now been cancelled. Accordingly, claims 23-50 are pending in this application. Reconsideration is respectfully requested.

Applicants wish to thank Examiner Sisson for conducting an interview with their representative, the undersigned, at the Patent and Trademark Office on August 9, 2001. A representative of the assignee, Jack Veuskens, was present at the interview. The courtesy shown by Examiner Sisson to applicants' representatives as well as his cooperation and assistance in drafting patentable claims are especially appreciated.

The following remarks summarize the discussion during the interview.

Applicants' representative reviewed the rejection in the office action dated March 22, 2001, and applicants' response to the office action in their amendment dated July 23, 2001. Examiner Sisson indicated that he understood the response.

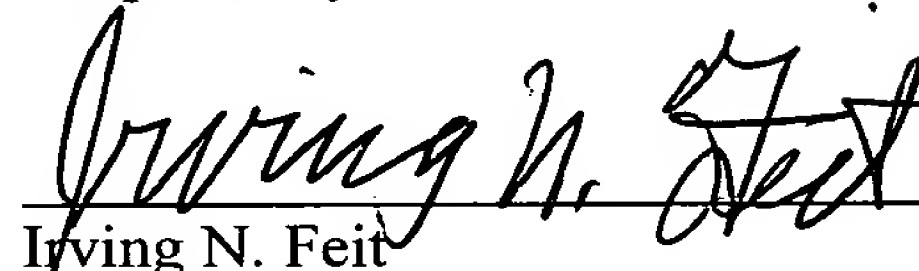
Examiner Sisson then stated that, upon reviewing the claims, he considered a final issue to relate to the breadth of the term "spacer" in claim 23. Examiner Sisson stated that the term did not have an upper limit on the number of atoms in the spacer.

Applicants and their representatives particularly appreciate the suggestion made by Examiner Sisson to rectify this problem. In particular, Examiner Sisson suggested the term "spacer means," thereby invoking the provisions of 35 U.S.C. §112, paragraph 6.

The claims have now been amended in accordance with the examiner's suggestion. As stated by the examiner in the interview summary, "...the disclosure had been found to set forth a variety of suitable spacers and as such, the claim would be limited to those spacers disclosed and the equivalents thereof; 35 U.S.C. §112, paragraph 6." The "variety of suitable spacers" may be found throughout the specification, for example, the spacers encompassed by the disclosure at page 4, line 28 to page 7, line 3.

This application is now believed to be in condition for allowance. Notice to that effect at the examiner's earliest convenience is respectfully requested.

Respectfully submitted,



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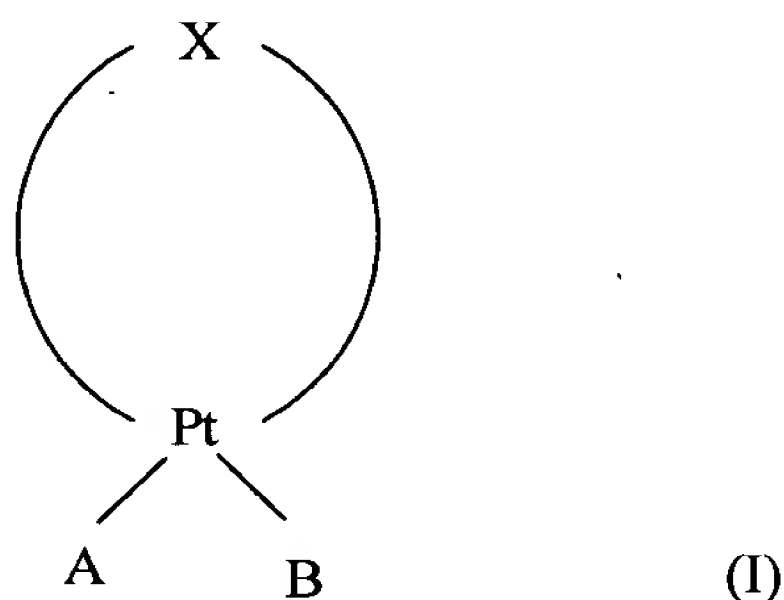
**VERSION OF AMENDMENT WITH MARKINGS**  
**TO SHOW CHANGES MADE**

Cancel claims 1-22 and add new claims 23- 105.

23. (Amended) A method for labeling a nucleotide comprising:

providing a spacer means, ~~comprising a chain having at least four atoms~~, a spacer reactive moiety at one end of the spacer means ~~chain~~, and an electron donating moiety at the other end of the spacer means ~~chain~~, wherein the spacer reactive moiety is capable of coupling the spacer means to a label when the spacer reactive moiety is reacted with the label;

providing a linker having formula I,



wherein X represents an aliphatic diamine, and A and B represent the same or different linker reactive moieties capable of reacting with the electron donating group of the spacer means or with the nucleotide, thereby attaching the spacer means or the nucleotide to the linker;

reacting the spacer reactive moiety with the label, thereby coupling the spacer means to the label;

reacting the electron donating moiety of the spacer means with one of the linker reactive moieties, thereby attaching the spacer means to the linker; and

reacting the nucleotide with the other linker reactive moiety, thereby attaching the nucleotide to the linker.

24. The method according to claim 23, wherein X represents an aliphatic diamine having 2-6 carbon atoms.

25. The method according to claim 23, wherein X represents an aliphatic diamine having the formula  $G_2NCH_2CH_2NG_2$ , wherein G represents H or an alkyl group of from 1 to 6 carbon atoms.

26. The method according to claim 23, wherein X represents ethylenediamine.

27. The method according to claim 23, wherein X represents N,N,N',N'-tetramethylethylenediamine.

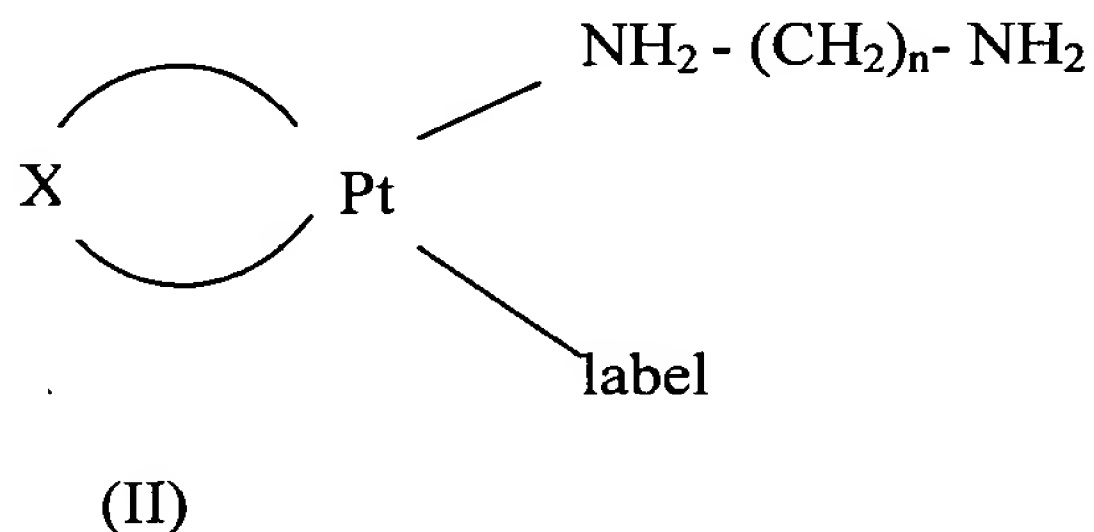
28. The method according to claim 23, wherein A and B represent  $NO_3^-$ ,  $SO_3^-$ ,  $Cl^-$ ,  $I^-$ , other halogen or  $Me_2SO$ .

29. The method according to claim 23, wherein A and B are the same.

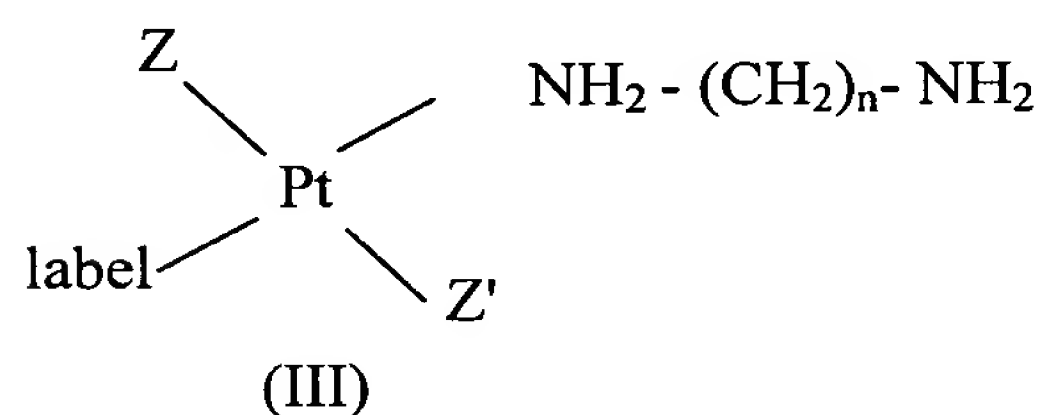
30. (Amended) The method according to claim 23, wherein the spacer means comprises no more than twenty carbon atoms.

31. The method according to claim 30, wherein the carbon atoms are non-branched.
32. (Amended) The method according to claim 23, wherein the spacer means comprises four carbon atoms and one heteroatom.
33. The method according to claim 32, wherein the heteroatom is oxygen.
34. (Amended) The method according to claim 23, wherein the spacer means is 1,8-diamino-3,6-dioxaoctane.
35. (Amended) The method according to claim 23, wherein the spacer means is an oligolysine or a polylysine.
36. The method according to claim 23, wherein the electron donating moiety is an amino group or a thiolate group.
37. The method according to claim 36, wherein the amino group is an aromatic amino group.
38. The method according to claim 36, wherein the amino group is an imidazole or purine group.
39. The method according to claim 23, wherein the spacer reactive moiety is  $\text{NH}_2$ .
40. The method according to claim 23, wherein the label is radioactive.
41. The method according to claim 23, wherein the label is an enzyme.

42. The method according to claim 23, wherein the label is a component of a specific binding pair.
43. The method according to claim 23, wherein the specific binding pair is biotin and avidin or streptavidin.
44. The method according to claim 23, wherein the label is a dye, a fluorochrome, or a reducing agent.
45. The method according to claim 23, wherein the label is digoxigenin.
46. The method according to claim 23, wherein the nucleotide is adenine, thymidine, cytosine, guanine, or uridine.
47. The method according to claim 23, wherein the nucleotide is adenine, thymidine, cytosine, and either guanine or uridine.
48. The method according to claim 23, wherein the nucleotide is a purine.
49. The method according to claim 23 wherein the linker is reacted with a labeling moiety comprising



or the formula



wherein X represents an aliphatic diamine, Z and Z' represent a non-leaving ligand and n is an integer of from 2 to 10.

50. A method according to claim 49, wherein Z and/or Z' represent an NH<sub>3</sub>, NH<sub>2</sub>R, NHR<sub>2</sub>, or NR<sub>3</sub> group, wherein R represents an alkyl group having from 1 to 6 carbon atoms.